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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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| 08/466,698      | 06/06/95    | SANSONETTI           | P 2356.0043-02      |

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18M1/0430

EXAMINER  
CAPUTA, A

ART UNIT  
1817

PAPER NUMBER

DATE MAILED: 04/30/97

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trad marks**

# Office Action Summary

Application No.

08/466,698

Applicant(s)

Sansone et al.

Examiner

Anthony C. Caputa

Group Art Unit

1817



☒ Responsive to communication(s) filed on Dec 20, 1996

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claims

☒ Claim(s) 1-10, 13, and 14 is/are pending in the application.

Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 1-10, 13, and 14 is/are rejected.

☐ Claim(s) \_\_\_\_\_ is/are objected to.

☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 12

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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#### DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1817.
2. Claims 1-10, 13, and 14 are pending.

#### *Specification*

3. The prior objection to the title is withdrawn in view of applicants' amendment

#### *Claim Rejections - 35 USC § 112 2nd paragraph.*

4. The prior rejection of claims 1-10 under 35 U.S.C. § 112, second paragraph, for the recitation of "substantially" and "substantial" is withdrawn in view of applicants' amendment

#### *Claim Rejections - 35 USC § 112/1st paragraph*

5. The following is a quotation of the first paragraph of 35 U.S.C. § 112:  
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach one skilled in the art how to make and/or use the claimed invention, i.e. failing to provide an enabling disclosure as set forth in the last Office Action.

As set previously, it is apparent that numerous modified Shigella are required to practice the claimed invention. That is, one skilled in the art can not make the claimed microorganisms

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or vaccines without the Shigella species which contain the claimed inactivated genes. Accordingly as a required element, the modified Shigella must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available the enable requirements of 35 U.S.C. § 112, first paragraph may be satisfied by the deposit of the claimed microorganisms and limiting the claims to the deposited mutants. See 37 C.F.R 1.802.

In the instant case the construction of claimed Shigella mutants requires knowledge of the nucleotide sequence of said genes, which regions are responsible for biological activity, and the number of nucleotides which must be deleted or inserted. Due to the limited teaching of the specification and the unpredictable nature of which mutations are useful one skilled in the art can not practice the invention as claimed absent undue experimentation. In view of the foregoing the only means by which applicants can provide an enabling disclosure for the Shigella mutants is by depositing said mutants and limiting the claims to the deposited mutants.

Applicants urge that the specification provides sufficient teachings for one skilled in the art to practice the claimed invention. Applicants state that the specification teach of methods of modification to employ in order to inactivate the genes. These arguments are not considered persuasive. The decisional law has held the mere recitation in the specification of a broad concept does not necessarily provide a sufficient basis for broadly claiming it (i.e. transposon mutagenesis). See Ex parte Gardner 157 USPQ 162 (Bd. Pat. Appls and Interf. 1967), In re Cavallilo, 127 USPQ 202 (CCPA 1969). The fact that the terms in a claim are the same as those in the specification does not prevent the claims from being rejected as unduly broad if they define subject matter not described to be the actual invention by means of adequate representative samples. See in re Lund, 153 USPQ 625 (CCPA 1967). In the instant case the construction of claimed Shigella mutants requires knowledge of the nucleotide sequence of said genes (iscA, virG, aerobactin, enterochelin), which regions are responsible for biological activity, and the number of nucleotides which must be deleted or inserted. Due to the limited

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teaching of the specification and the unpredictable nature of which mutations are useful one skilled in the art can not practice the invention as claimed absent undue experimentation. In view of the foregoing the only means by which applicants can provide an enabling disclosure for the Shigella mutants is by depositing said mutants and limiting the claims to the deposited mutants.

While it would appear techniques are known in the art for inactivation, as pointed out by applicants it is not routine in the art to screen for positions within the DNA sequence of the gene so that it does not invade the cells, spread within infected cells, or not produce toxins. Because the specification does not disclose :

- which regions of the genes are responsible for biological activity;
- the number of nucleotides which must be deleted or inserted;
- the identity of the genes that are responsible for invading cells, not producing toxins, etc.;
- more than one genes would be expected to be involved in toxin production, spreading, and/or invasion;
- no guidance as to which of the essentially infinite possible choices is likely to be successful;

modifications that can be made to inactivate the genes is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986).

Beyond the reasons set forth above, while it may be true that the prior art teaches of *iscA*; *virG*; *aerobacterin*; *enterocholin*, and the Shiga toxin gene as set forth by applicants said evidence is not commensurate in scope with the claimed invention which encompasses the inactivation of gene responsible for invasion, spreading, and toxin production.

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Applicants argue that a deposit is not required since the specification is clearly enabled. Applicants argument is not persuasive. It is the Examiner position that the specification is not enabled for the reason set forth above.

6. Claims 1-10, 13, and 14 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

***Claim Rejections - 35 USC § 102***

7. The prior rejection of claim 13 under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Sekizaki et al. (Infection and Immunity 55(9):2208-2214 1987) is withdrawn in view of applicants' amendment.

***Claim Rejections - 35 USC § 103***

8. The prior rejection of claims 1-10 under 35 U.S.C. § 103 as being unpatentable over Mills et al. in view of Sekizaki et al., Nassif et al., Makino et al., and Ozenberger et al. is withdrawn in view of applicants' amendment.

***Claim Rejections -Double Patenting***

9. The prior provisional rejection of Claim 13 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 39 of copending application Serial No. 08/118,100 is maintained.

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Although the conflicting claims are not identical, they are not patentably distinct from each other because both are drawn to *Shigella* mutant which has an inactivated Shiga toxin gene (Shiga-toxin A).

Applicants request to hold this rejection in abeyance until allowable subject matter has been indicated. Applicants argument is noted. However, since no allowable subject matter has been indicated the prior provisional rejection of claim 13 under the judicially created doctrine of obviousness-type double patenting is maintained as set forth in the last Office Action.

#### **NEW GROUNDS OF REJECTION**

10. Claims 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Newly amended claim 13 and dependent claims thereof are rejected for lack of antecedent basis for use of the term "the genes". It is suggested by the Examiner that applicants amend this phrase to "the gene" to obviate said rejection.

#### ***Conclusion***

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire **THREE MONTHS** from the date of this action. In the event a first response is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period

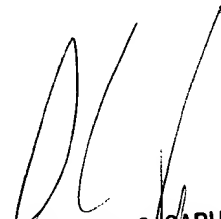
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will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Anthony C. Caputa, whose telephone number is (703)-308-3995. The examiner can be reached on Monday-Thursday from 8:30 AM-6:00 PM. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703)-308-0196.

Papers related to this application may be submitted to Art Unit 1817 by facsimile transmission. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The Fax number is (703)-308-4242

Anthony C. Caputa, Ph.D.  
April 2, 1997



ANTHONY C. CAPUTA  
PRIMARY EXAMINER  
GROUP 1800